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TITLE: A Randomized Clinical Trial of Cognitive Behavioral Treatment for PTSD in Women

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<b>13. SUPPLEMENTARY NOTES</b>					
<b>14. ABSTRACT</b>  This study is a randomized clinical trial comparing two types of individual psychotherapy for treating Posttraumatic Stress Disorder (PTSD) in 284 female veterans and active duty personnel at 11 VA sites and one DoD site. Prolonged Exposure and Present Centered Therapy are the two treatment conditions, the former a trauma-focused approach and the latter an approach focused on how the individual is functioning currently. The hypothesis is that Prolonged Exposure therapy will be more effective than Present Centered Therapy for alleviating the symptoms of PTSD in female veterans and active duty personnel. Data collection is nearing completion and data analysis is expected to be finished in 2006. 71% of the participants completed all treatment sessions and nearly 80% completed all follow-up assessments. There are no conclusions to date.					
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## INTRODUCTION

The study is a randomized single-blind clinical trial comparing two types of individual psychotherapy for the treatment of Posttraumatic Stress Disorder (PTSD) in women. This is a VA Cooperative Study. Walter Reed Army Medical Center is the only participating DoD site. Eleven VA sites around the U.S. participated in this trial. One VA site, Bay Pines, Florida, withdrew in December 2003. The enrollment goal for each site was 32 participants over 24 months of active recruitment in the study. All research data are compiled and analyzed at the VA Cooperative Studies Program Coordinating Center (VA CSPCC) in Palo Alto, CA and will not be shared with the individual sites until completion of the study.

The objective of this clinical trial is to evaluate the efficacy of Prolonged Exposure (PE) therapy for treating PTSD and associated problems in active duty and veteran women. The hypothesis is that PE will be more effective than Present Centered Therapy (PCT) for treatment of PTSD in female veterans and active duty personnel. The primary outcome in this study is PTSD severity at the 3-month follow-up assessment as measured by the Clinician Administered PTSD Scale (CAPS), a diagnostic interview that captures PTSD symptom severity.

The treatments are a trauma-focused approach, PE, and an approach focused on current needs and problems, PCT. Both treatment conditions consist of 10 weekly 90 minutes sessions. PE procedures include education about common reactions to trauma, breathing retraining, prolonged (repeated) exposure to trauma memories, repeated in vivo exposure to situations the patient is avoiding due to trauma-related fear, and discussion of thoughts and feelings related to exposure exercises. The goal of PE is to reduce the individual's emotional response to the traumatic event or feared stimuli through habituation. PCT is designed to provide emotional support for the trauma victim with emphasis on the individual's current life. The goal of treatment is to reduce distress and to increase a sense of mastery in day-to-day life.

The work will significantly expand knowledge about the treatment of PTSD in military women. The methodology for the study is summarized as follows: All participants, including self-referrals, will enter the study through referral by mental health clinicians. Following informed consent, participants will be screened for inclusion and exclusion criteria. If they meet these criteria and agree to participate, they will be randomly assigned to one of the two treatments, which will occur weekly for 10 weeks. Subjects will be assessed before treatment, immediately following treatment, and 3 and 6 months after the end of treatment. That data will be compared between the two treatment groups.

## BODY

Participant recruitment began in August of 2002 at the VA sites (see Table 1 for recruitment timeline by site). In the multi-site study, a total of 284 participants were randomized as of August 2004 (see Table 2 for a breakdown of enrollment by site). The mean age of the female participants is  $44.8 \pm 9.4$  with a range from 22 to 78 years. Fifty-five percent (55%) of the participants are Caucasian and 62% are college educated.

A total of 284 randomized participants began study treatment with 201 (71%) of them completing all 10 treatment sessions (see Table 3 for a list of the traumatic events the participants addressed in treatment). As of October 2005, approximately 16 participants remain in the follow-up assessment phase. During the course of this trial, sixty-six (66) participants voluntarily terminated treatment. Two hundred thirty five (235) participants completed the first post-treatment assessment, 230 completed the 3-month follow-up assessment, and 213 completed the 6-month follow-up assessment. Information regarding the numbers of patients receiving either PE or PCT are kept by the VA CSPCC and not shared with the individual study sites in this double blind protocol.

A total of twenty - seven (27) subjects completed informed consent at the WRAMC site. Three (3) subjects consented to Practice Assessments only. Ten (10) women signed informed consent to be a training case. Six (6)

of them completed their assigned treatment. One (1) did not complete the ten treatment sessions within the prescribed timeframe of twenty weeks. One (1) was the subject of an SAE which was reported in the 2002 APR. Two (2) subjects dropped out during the assessment phases.

Fourteen (14) subjects consented to be randomized at WRAMC. Seven (7) of these subjects dropped out prior to being randomized. Data collection on the seven (7) WRAMC randomized participants is complete. Two (2) participants completed all treatment sessions and all three follow-up assessments. Two (2) participants completed treatment and two follow-up assessments. One (1) participant voluntarily withdrew from treatment after five sessions. One (1) completed treatment but did not agree to follow-up assessments and was the subject of an AE reported in the 2003 Annual Progress Report. One (1) subject was deployed overseas with Operation Iraqi Freedom one week after being randomized and did not receive any of the treatment protocol.

The average age of the WRAMC participants was 41 years with a range of 29 to 64 years of age. Six (6) women were Caucasian and six (6) were African American. Two (2) were Hispanic and one (1) was Native American. Six (6) were college graduates, six (6) completed some college, two (2) had professional degrees, and one (1) completed high school. Seven (7) were single, four (4) were married, three (3) were divorced, and one (1) was separated.

There have been 17 Serious Adverse Events (SAE) among the 284 randomized participants during this study. Three (3) involved suicide or homicide attempts, twelve (12) were psychiatric hospitalizations, and two (2) were deaths unrelated to the study (one of a drug interaction confirmed by autopsy and one is being investigated as a homicide). There were an additional 8 SAEs among the multi-site study's 138 therapist training cases.

No active trial participant at the WRAMC site experienced an SAE. A randomized patient at the WRAMC site experienced an increase in her PTSD symptoms during her study treatment. This decompensation was reported to WRAMC DCI and the HSRRB and was not considered an SAE. Thus far, the independent Data Safety Monitoring Board has not noted any association between the study intervention and SAEs and the rate of SAEs is generally low.

Study-wide terminations are as follows: Seventeen (17) subjects dropped out of the study after being randomized, but before receiving any study treatment. Twenty-two (22) subjects were terminated during the active treatment phase for adverse events or failing to complete the treatment within the prescribed timeframe. Forty-four (44) subjects dropped out of treatment during the active phase. Twenty-six (26) subjects terminated during the follow-up assessment phase.

#### *KEY RESEARCH ACCOMPLISHMENTS*

- 284 randomized participants in the multi-site trial
- 7 randomized participants at the WRAMC site
- 71% of randomized participants completed treatment
- 83 % of randomized participants completed post-treatment assessments
- 81% of randomized participants completed the 3-month follow-up assessment
- 75% of randomized participants completed the 6-month follow-up assessment
- Participants report high levels of satisfaction with treatment approaches (see Table 4)
- On average, participants experienced PTSD symptom reductions (see Table 5 and details listed below)
- WRAMC site received a total of 117 prospective participant referrals
- WRAMC study staff provided referrals to mental health practitioners in the DoD and VA system for all ineligible prospective participants

## RESEARCH PERSONNEL

Employee	Title/Position	Dates of Employment
Lolita Davenport	Site Coordinator	September 2001 - May 2002
Renee Clauselle, Ph.D.	Site Coordinator	June 2002 - November 2002
Denise Gonzalez, LGSW	Site Coordinator	January 2003 - April 2005
Phyllis Betts, LGS W	Assessment Technician	October 2001 - July 2003
Nancy Meyer, LICSW	Assessment Technician	July 2003 - May 2004
Kristie Gore, Ph.D.	Assessment Technician / Site Coordinator	July 2004 - October 2005

## REPORTABLE OUTCOMES

All analyses are being conducted by the VA Cooperative Studies Program Coordinating Center. Because outcome data is not yet available, this information is reported for the WRAMC site only. The multi-site investigators plan to assemble a number of manuscripts for publication based on the outcome data once it is compiled.

Preliminary findings regarding treatment-related symptom reductions are represented in Table 5. The a priori dependent variables are the symptom score reductions between pretreatment baseline scores and the 3-month follow-up period. These data indicate CAPS scores decreased by an average of 23.6 points. Participants reported an average of a 10 point symptom reduction on the PTSD Symptom Scale (PCL) and a 4 point score reduction on the Beck Depression Inventory (BDI). Only means and standard deviations were observed by the VACSPCC data analysis team. The statistical and clinical significance of these symptom reductions remain unknown.

### Presentations:

Sheliga, Vivian; Engel, Charles; Gonzalez, Denise; Woodard, Pamela. **Special Care for Special Women. A PTSD Treatment Trial For Women: Challenges and Lessons Learned.** Sixth Annual Force Health Protection Conference, US Army Center for Health Promotion & Preventive Medicine, Albuquerque, New Mexico, August 2003.

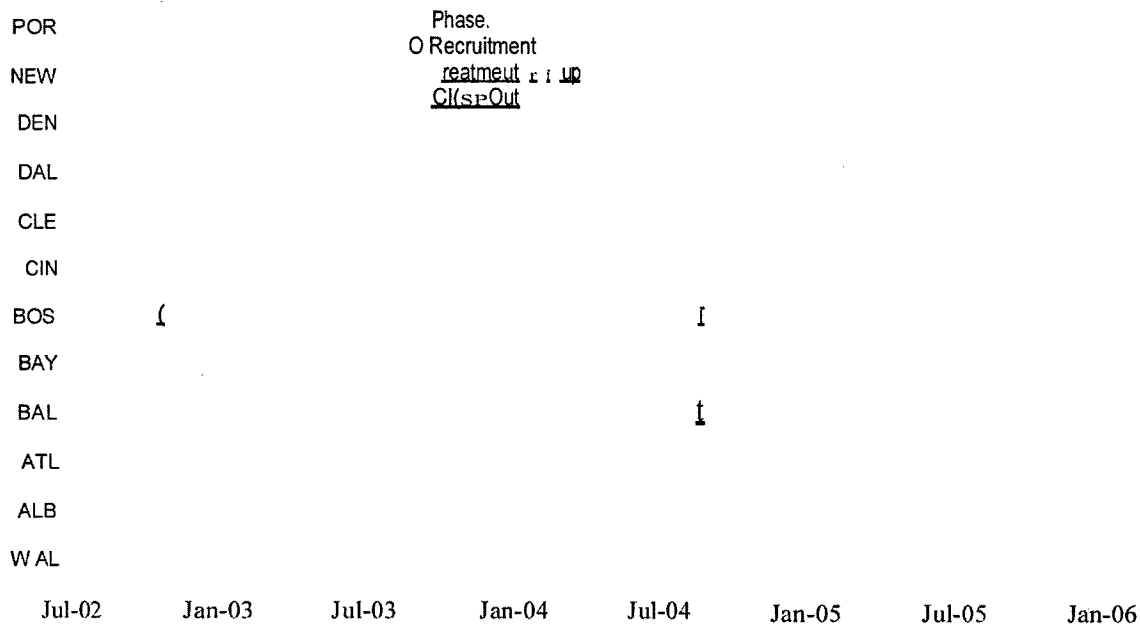
Gonzalez, Denise; Meyer, Nancy; Gore, Kristie; DeDeyn, Judy; Bruner, Victoria, Peterson, Catherine; Engel, Charles. **The Care of Military Women with Traumatic Stress Concerns: What They've Said and What We've Learned.** Seventh Annual Force Health Protection Conference, US Army Center for Health Promotion & Preventive Medicine. Albuquerque, New Mexico, August 2004.

Gonzalez, Denise; Meyer, Nancy; Gore, Kristie; DeDeyn, Judy; Bruner, Victoria; Peterson, Catherine; Engel, Charles. **Post Traumatic Health Care Needs: What do Military Women Say?**, International Society for Traumatic Stress Studies, Annual Conference, New Orleans, Louisiana, 2004.

## CONCLUSIONS

No conclusions are available at this time. The study continues at several sites through December, 2005. All data is compiled and analyzed at the VA Cooperative Studies Program Coordinating Center. Data analysis is not expected until 2006. A preliminary look at the data indicated participants experienced an overall decrease in PTSD symptoms and a slight reduction in depression symptoms at the 3-month follow-up assessment.

Table 1. Study Timeline (2 years of recruitment, 1/2 year of follow-up).

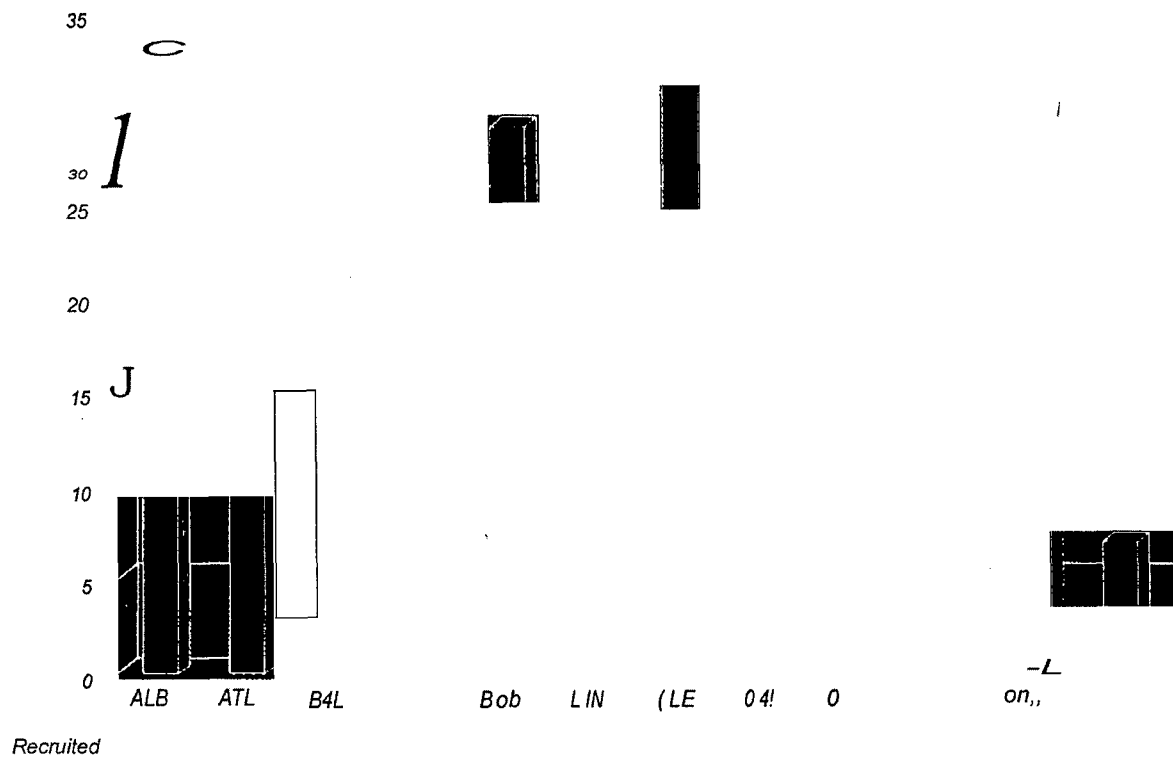


The 12 study sites have 256 months of recruitment out of the total of 264 (avg. = 21.3 months/site)

Key:

POR = Portland VA Medical Center  
 NEW = New Orleans Medical Center  
 DEN = Denver VA Medical Center  
 DAL = Dallas VA Medical Center  
 CLE = Cleveland VA Medical Center  
 CIN = Cincinnati VA Medical Center  
 BOS = Boston VA Medical Center  
 BAY = Bay Pines VA Medical Center  
 BAL = Baltimore VA Medical Center  
 ATL = Atlanta VA Medical Center  
 ALB = Albany VA Medical Center  
 WAL = Walter Reed Army Medical Center

Table 2. Recruitment by Site (N=284)



\* Bay Pines withdrew from enrollment on Aug'03, and close Dec'03

Key:

POR = Portland VA Medical Center  
 NEW = New Orleans VA Medical Center  
 DEN = Denver VA Medical Center  
 DAL = Dallas VA Medical Center  
 CLE = Cleveland VA Medical Center  
 CIN = Cincinnati VA Medical Center  
 BOS = Boston VA Medical Center  
 BAY = Bay Pines VA Medical Center  
 BAL = Baltimore VA Medical Center  
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 ALB = Albany VA Medical Center  
 WAL = Walter Reed Army Medical Center



Table 3. Traumatic events addressed in treatment (N = 284)

<u>Index Trauma:</u>	
Sexual Assault*	66%
Physical Assault	14%
» Combat/Expo to War-zone	6%
» Transportation Accident	2%
Assault with a Weapon	2%
Other Unwanted Sexual Exp*	2%
Sudden Violent Death	1%
Sudden Death of One Close	1%
Other	6%

\* -70% of these index sexual traumas considered are Military Sexual Trauma (MST)

Table 4. Participant Satisfaction Ratings (N = 284). Median scores reported.

Satisfied with Treatment Received (1-7)	1
Between "1. very satisfied" & "2. moderately satisfied"	
Present Condition (1-7)	3
Between "3. good" & "4. fair"	
Changed since Beginning Treatment (1-7)	2
Between "2. somewhat better" & "3. little better"	
Condition Related to Treatment (1-5)	5
Between "4. probably related" & "5. definitely related"	

Table 5. Assessment summary - mean change in symptoms across conditions.

	Phase-3 (baseline)	1-week Post	3-month f/u	6-month f/u
CAPS	78.3±16.4	57.8±27.3	54.7±27.3	53.8±28.8
PTSD Checklist Score	57.6±12.6	46.4±16.7	47.4±16.8	47.0±17.0
Beck Depression Inv.	24.6±9.5	19.4±11.6	20.7±11.7	19.7±12.1
Spielberger Anxiety Inv.	52.3±13.4	49.0±15.0	50.8±14.7	50.3±14.8
ASI: Alcohol Use	0.04±0.09	0.03±0.07	0.04±0.10	0.04±0.10
ASI: Drug Use	0.00±0.02	0.00±0.02	0.00±0.01	0.00±0.01
Quality of Life Inventory	0.1±1.9	0.4±2.1	0.3±2.1	0.3±2.2